REMARKS

Reconsideration of this Application is respectfully requested.

Claims 51 and 60-292 are currently pending. Claims 80-292 have been withdrawn.

Claims 70-72 have been cancelled and 51, 60-67, 69 and 73-77 have been amended. These changes do not introduce new matter and entry of the amendments is respectfully requested.

As a preliminary matter, Applicants acknowledge and appreciate the withdrawal of the previous rejections under 35 U.S.C. §112, first and second paragraph and the acceptance of the amendments to the figures and specification.

Election of Species

Applicants acknowledge the election of species SEQ ID NO:6 and that Claims 51 and 60-79 read on the elected species and are under examination. The claim status identifiers have been updated to reflect the previously made election of species, without prejudice to refiling of claims of the original scope.

Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 60-79 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. More specifically, the Office Action states that the claims are not enabled for the claimed method beyond polypeptides other than SEQ ID NOs: 3 and 6.

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without undue experimentation (e.g., In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991). An invention is enabled even though the disclosure may require some routine experimentation to practice the invention. Hybritech Inc. V. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Applicants have amended the claims herein to recite methods for protecting cells, organs or tissues comprising exposing the cells, organs or tissues to an immunoprotective amount of a

polypeptide comprising the amino acid sequence presented as SEQ ID NO:3 or SEQ ID NO:6 or a polypeptide having substantial sequence identity to the amino acid sequence presented as SEQ ID NO:3 or SEQ ID NO:6 and the immunoprotective properties of the polypeptide presented as SEQ ID NO:3.

Applicants submit that the current claims are consistent in scope with the disclosure, given that the claims require the polypeptide employed in the method exhibit the immunoprotective properties of the polypeptide presented as SEQ ID NO:3. In view of the above amendments and remarks, withdrawal of the enablement rejection under 35 U.S.C. § 112 is respectfully requested.

Rejection Under 35 U.S.C. §102(b)

Claims 51 and 60-79 stand rejected under 35 U.S.C. §102(b) as being anticipated by Hope et al., 1995, IDS. Applicants respectfully request that the examiner provide a copy of the 1995, Hoppe et al., abstract. To Applicants knowledge, a 1995, Hoppe et al., abstract reciting SEQ ID NOs 3 or 6 was not cited in an IDS submitted in this case.

For anticipation under 35 U.S.C. §102, the reference "must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP §706.02). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Examiner has not met the burden of proving inherent anticipation. The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not

necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

The present claims are based on the activity of a human Hsp47-related immunoprotective polypeptide. Furthermore, the independent claims require that the cell, tissue or organ damage is mediated by the immune system ("the polypeptide is effective to prevent damage caused by lymphocytes, NK cells or NK-like cells"), such as occurs with organ transplants or autoimmune disease. This is an important feature since it excludes any damages caused by artificial cells not actively involved in the immune system activities.

Further Applicants submit that there was no enabling disclosure in cited art regarding the production of isolated recombinant HSP47 polypeptides and nucleic acids. Applicants submit that the human HSP47 polypeptide and nucleic acid sequence was both novel and inventive as of the priority date of the subject application. The instant specification describes in detail the technical difficulties in producing recombinant HSP47 polypeptides and nucleic acids in the laboratory, reliant upon the use of an unconventional cloning technique.

The cited reference only describes certain results which are not enabling for the scope of the current claims. Applicants are not presently claiming the HSP47 polypeptide sequence in

isolation but a method for reducing immune-mediated damage to cells, tissues or organs comprising contacting a cell, tissue or organ with an immunoprotective amount of an isolated polypeptide having the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:6, wherein the immune-mediated damage is caused by lymphocytes, NK cells or NK-like cells.

Applicants are aware of a November 1995 Hope et al. abstract from Blood which provides very limited disclosure relative to the treatment of HUVEC cells with Brefeldin A which renders them resistant to activated CD3+ CD56+ CIK. Furthermore, the abstract reports that treatment of HUVEC with Brefeldin A induces cell membrane expression of a glycoprotein (p46) that may represent a human form of Hsp47. This does not constitute an enabling disclosure relative to the instant claims. The current invention is based on identification of polypeptides with protective properties against immune-system mediated cell damage. The use of human Hsp47, and identification of an active fragment thereof was not disclosed nor is it obvious in the light of the November 1995 Hope et al. abstract.

The November 1995 Hope et al. abstract does not teach one of skill in the art how to make or use human Hsp47 (SEQ ID NO:6) or the use of AVLSAEQLR (SEQ ID NO:3) in a method for reducing immune-mediated damage to cells, tissues or organs by contacting the cell, tissue or organ with SEQ ID NO:6 or SEQ ID NO:3, wherein the immune-mediated damage is caused by lymphocytes, NK cells or NK-like cells. The prior art lacks enablement for both expression, purification, isolation and use of human Hsp47, as required by the current claims.

The prior art does not teach one of skill in the art how to perform an assay in a relevant model to test the function and pharmaceutical properties of human Hsp47 in a physiological environment such that one could determine if the polypeptide is effective to prevent damage caused by lymphocytes, NK cells or NK-like cells.

Although the November 1995 reference mentions human Hsp47, it does not enable the skilled person to practice the claimed invention absent further instruction. Such instruction is not provided in the cited abstract and was not present in the art at the time the application was filed.

Even if the skilled person had tried to clone and express human Hsp47, there was not a reasonable expectation of success based on the prior art. At the priority date it was possible to

clone gene cassettes without major problems from PCR products based on mRNA templates, however, in the case of human Hsp47 this had not been accomplished. After endless unsuccessful assays with standard approaches, cloning of Hsp47 was achieved by the inventors of the instant application with a nonobvious cloning strategy that in an uncommon fashion referred to the use of the complete small PCR product as a primer for a larger PCR product and specifically designed site-directed mutagenesis as well as further sequence modifications to allow the coding frame to be cloned (please refer Example 2 of application).

Accordingly, Applicants respectfully submit that the prior art does not anticipate, nor does it render obvious, Claims 50 or 60-79. Withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 70-72 and 74-77 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

The Patent Office guidelines state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Indeed, as set forth in the MPEP: a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc .*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Claims 70-72 have been cancelled and Claims 74-77 have been amended to clarify that the claimed methods rely on polypeptides which exhibit the immunoprotective properties of SEQ ID NO:3. The claims also make reference to sequences have specific percentage identity with

the sequences set forth in Figure 1. Support for this claim language is provided at least on page 10, lines 3-12 and page 12, lines 1-15.

In view of the specific examples and general guidance provided by Applicants, one of skill in the art could readily determine that the Applicant was in possession of the claimed sequences at the time the application was filed. Withdrawal of the written description rejection is respectfully requested.

Conclusion

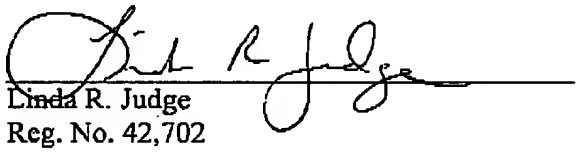
Claims 51 and 60-79 are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested.

The Commissioner is authorized to charge any additional fees that may required, or credit any overpayment, to DLA Piper US LLP Deposit Account No. 07-1896 **(Order No. 030673)**.

If any issues remain which the Examiner feels may be best resolved through a personal or telephonic interview, the Examiner is respectfully requested to contact Applicants' counsel, Linda R. Judge at (415) 836-2586.

Respectfully submitted,

Date: October 10, 2006



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